11.

Spontaneous Neoplasms in Fishes. III. Lymphosarcoma in *Astyanax* and *Esox*.

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(Plates I-XI.)

INTRODUCTION.

Lymphosarcoma, or any disease involving lymphoid tissues, whether neoplastic or not, is rare in fishes. Several cases have been recorded in the literature but very few histological or cytological details have been given. Johnstone (1912) reported an intraorbital lymphosarcoma which had its original locus in the chorioid layer. The growth on a female European flounder (*Pleuronectes flesus*) involved the left eye which was conspicuously protruded as a mass measuring 21 × 20 mm. The cornea was nearly opaque, anterior and posterior chambers were fused, iris was completely destroyed and the lens was lying detached in a mass of leucocytes and blood cells. Histologically, the growth consisted of a loose, delicate, fibrous connective or elastic tissue which gave rise to a still more delicate reticulum containing great numbers of lymphocytes. The latter were of two sizes; the smaller and more numerous had very little visible cytoplasm, the larger and less numerous a comparatively greater amount of cytoplasm. The growth was further characterized by the presence of large lymphatic spaces, very few blood vessels and a mild inflammatory reaction. The sclerotic coat was incomplete; there was no trace of the chorioid layer and very little of the pigmented layer of the retina remained. There was no evidence of metastases, and Johnstone believed that the growth was a primary one.

In 1926, Johnstone reported another case of lymphosarcoma in a herring measuring about 30 cm. in length. The growth consisted of two masses within the body cavity which were supported by thin folds of peritoneum. The larger mass measured about 50 mm. in length and 25 mm. in width. Histologically the major part of the growth presented the same picture as in the flounder. However, other areas in the mass showed spindle-shaped cells arranged concentrically and as whorls. The smaller growth, measuring about 15 × 5 mm., was reddish in appearance. The color resulted from a plexus of blood vessels on its external surface, giving the growth the appearance of a hemolymph gland. Histologically this was similar to the large mass, but according to Johnstone, there was "a general tendency for the leucocytes to take on the sarcomatous, short spindle form," replacing the fibrous reticulum. No gonads were present although the fish was of a size that normally would have them. Johnstone believed that the reproductive glands had become involved in the lymphosarcomatous growth, "so that all traces of their original structure have become obliterated."

Plehn (1924) reported a lymphosarcoma in a goldfish. This case was the only one recorded by Thomas (1931) in his collected data on fish tumors, and probably the one referred to by Schäperclaus (1935) in his general discussion on fish neoplasia. According to Plehn, the fish showed an enormous ventral swelling, exophthalmia and raised scales. On autopsy it was found that the body cavity was filled with fluid and other conditions were present that are normally associated with renal dysfunction. Histologically the kidney showed a considerable proliferation of leucocytes which caused a great deal of destruction of the epithelial cells of the urinferous tubules. In certain areas, the lymphocytes had invaded the lumen of the tubules, causing considerable dilation of various segments, including Bowman's capsule. Blood vessels were thrombosed. Metastases into the liver had occured, infiltrating the parenchyma where compact lymphoid foci were set up, resulting in necrosis of the invaded areas. Neoplastic cells were also found in lymphatics and sinusoids.

A lymphosarcoma of the kidney of a fully grown female conger eel was reported by Williams (1931). Apart from a large ventral swelling, no other manifestations were noted. On dissection it was found that the swelling was due to a large oval, balloon-

like mass in the posterior part of the body cavity which measured 16.6 cm. in length, 7.8 cm. in width and 0.6 cm. in height. Numerous blood vessels were noted on the ventral surface of the growth. Histologically most of the growth was composed of great numbers of lymphocytes supported by a thin meshwork of reticular fibers. The uriniferous tubules were widely separated and greatly compressed. The growth was characterized further by a thickening of the fibrous covering with some indication of penetration by lymphocytes. Williams believed that the growth had developed fairly rapidly, and although it possessed infiltrative powers, its activities appeared to be purely local.

The present contribution deals with descriptions of lymphosarcomas in two species of fishes. They are considered separately because the origin and processes involved are distinct. In the pike, *Esox lucius* Linnaeus, the neoplastic cells were of the large lymphoblast type with the primary origin in the kidney. The growth in the characin, *Astyanax mexicanus* (Filippi), consisted mainly of typical lymphocytes with the primary origin probably in the thymus-like lymphoid tissue in the posterior branchial region.

The writer wishes to thank Dr. G. M. Smith for assistance in the preparation of the pike material, and Dr. C. M. Breder, Jr., and Miss Priscilla Rasquin of the American Museum of Natural History for the *Astyanax* and for histological material of related fishes.

1. Lymphosarcoma in the Pike.

A preliminary report of this disease in the northern pike, *Esox lucius* L. (= *Esox estor*), was given by Nigrelli (1943). Twelve fully grown fish succumbed at various intervals, particularly in the summer months, at the New York Aquarium during the years 1940 and 1941. Five females and one male were six years old, two females and one male were three years old, and three females were two years old. There were no external manifestations of the disease, but autopsies showed comparatively massive growths on the kidney (Plate I, Figure 1) and "abscesses" or nodules in the liver (Plate I, Figure 2). The kidney growths were in some instances grayish and granular in appearance with practically the entire posterior part of the organ involved. In other cases, the growths were nodular. Frequently both types were present on the same kidney and often continuous with one another. The granular stage may be a later manifestation of the disease (Plate I, Figure 4).

The material was fixed in 10% formalin and sectioned in paraffin from six to ten microns. Harris' and Delafield's hematoxylin-eosin, Giemsa's and Mallory's tripl stains were used.

Histologically the growths in the kidne were identified as lymphosarcomas. The nec plastic cells were mainly of the large lym phoblast type supported by irregular strand of fibrous stroma and a very delicate retic ulum (Plates I-III). In some areas th amount of fibrous tissue was so extensiv as to border on a fibrosis (Plate III, Fig ures 10 and 12; Plate IV, Figure 13). Th cells varied in size and shape. Toward th center of the mass they were more or les flattened, but in other areas they were usu ally rounded or polyhedral in appearanc (Plate II). The nuclei of these cells wer vesicular, spherical or bean-shaped and usu ally eccentric in position. The chromati was granular, varying as to number an size of granules. The cytoplasm was mor or less homogeneous, but the staining reac tion varied somewhat as demonstrated i those sections stained with Giemsa's. In th majority of cells with comparatively mor cytoplasm, the staining reaction was slight ly acidophilic. In other cells with lesse amounts of cytoplasm the reaction was de cidely basophilic. Granulocytes and transi tional cells, commonly present in the norma teleost kidney, were not seen. Occasionally small groups of typical lymphocytes wit hyperchromatic nuclei together with few bu widely scattered plasma cells were present Giant cells typical of certain human lym phosarcomas were lacking. However, occa sionally an uninucleate or binucleate "giant" cell with hyperchromatic nuclei was seen.

Cytoplasmic or intranuclear inclusion were not seen, nor was there any evidence of parasitic infection to which these fis are often susceptible.

There was much evidence of great activ ity of the neoplastic cells. Numerous mi totic figures in various stages were found throughout the growth (Plate II, Figure 7). The tubules were often constricted by the advancing lymphoblasts (Plate I, Fig ures 3 and 4; Plate II, Figure 8; Plate III Figure 9) which in some instances gave the false impression that a hyperplasia of the renal elements was present (Plate I, Fig ure 3), as was interpreted by Nigrell (1943). In many places the lumen was com pletely occluded or the tubules and glomer uli were invaded, destroyed and replaced by the lymphoid cells (Plate IV, Figure 14) This was especially evident in the granula type of tissue where only a relatively few tubules and glomeruli remained. Those tha were present were widely scattered o crowded into limited areas of the kidney (Plate I, Figure 4). In certain regions hy perplastic growth of reticular cells had tak en place, giving such areas the appearanc of a reticulum type of lymphosarcoma. I

both the nodular and granular growths, the blood vessels were considerably thickened and thrombosed (Plate I, Figure 3). The fibrous elements were particularly noticeable toward the periphery of the growth, especially in the granular type of tissue (Plate III, Figures 10-12; Plate IV, Figure 13). The lymphoid cells from the outer edge of the kidney had proliferated out, giving rise to new loci. Such regions gave the appearance of follicular lymphoblastoma (Plate III, Figure 11). These areas were characterized by the paucity of blood vessels and other hemal elements. The lymphoid cells around the periphery of the follicles were more or less similar to those from the kidney, whereas those located in the center of the follicles were invariably necrotic.

Metastatic growth occurred in the spleen and liver. Although the spleen was not especially enlarged, invasion nevertheless had taken place. Sinusoids were invaded and distended by the neoplastic cells. The outstanding feature in the spleen, however, was the extensive development of "pulp cords" (Plate V, Figure 17). In some areas the neoplastic cells had broken through the capsule and infiltrated into the surrounding fat and into the retroperitoneal region (Plate V, Figure 18). Metastasis into the liver in all probability took place through the portal systems. There was considerable involvement of this organ. Grossly, the lesions appeared as "abscesses" or nodules (Plate I, Figure 2) on the surface of a more or less cream-colored liver. The gall bladder was distended (Plate I, Figure 2) and filled with bile of watery consistency. Histologically the nodules were composed of compact masses of lymphoid cells supported by a reticulum and fibrous material (Plate IV, Figures 15 and 16). The growth in the liver presented a more pleomorphic picture than that present in the kidney. Although a number of mitotic figures were encountered, karyorrhexis was much more common. The neoplastic cells in the surrounding parenchyma completely disarranged the orderly formation of liver tubules. The advancing growth compressed the tubules so that they appeared as "cords" composed of varying numbers of cells (Plate IV, Figure 16). Certain cytological changes occurred in the liver cells. The nucleus and cytoplasm stained more intensely, and many of the cells were highly vacuolated with the nucleus pushed to an eccentric position.

2. Lymphosarcoma in Astyanax.

The fish involved was a male characin, *Astyanax mexicanus* (Filippi), which measured about 50 mm. in total length. It was one of many bred and raised by Dr. C. M. Breder, Jr., at the American Museum of Natural History from stock originally taken from the waters of Rio Tampaon, San Luis Potosi, Mexico. According to Dr. Breder's records the fish was hatched in 1942; it was approximately four years old when it was turned over to the writer in November, 1946. The external manifestations of the growth, such as enlargement of the area around the branchial region and exophthalmia (Plate V, Figure 19), had been first noticed about two months previously. When the fish was brought to the Aquarium's laboratory it was kept under observation for about three days. During this period it had acclimated itself to the new environment and all activities relative to handling, light, swimming, feeding, etc., were not unusual. The movements of the fish, either in the tank or when handled with a net, were vigorous and not those one would expect to find in a moribund fish. It was finally sacrificed, fixed in Bouin's and decalcified; paraffin sections were cut at thicknesses varying from 5 to 10 microns. The stains employed were Heidenhain's iron-hematoxylin and Delafield's hematoxylin with eosin, Masson's, Mallory's and Giemsa's.

The major part of the growth was a comparatively large mass of lymphoid cells supported by a delicate reticulum which extended into the left branchial cavity and was responsible for the swollen appearance of this region in the living fish (Plate VI, Figure 20). The origin of this growth was in all probability the thymus-like lymphoid "gland." A pair of such structures are normally present in the posterior region of the branchial cavity in juxtaposition to the last gill arch (Plate XI, Figure 38).

There was considerable local proliferation involving practically all the osseous, cartilaginous and muscular elements of the hyoid apparatus and related branchial structures (Plates VI and VII, Figures 22 and 23). There was also a direct invasion of the epithelium of the mucous membranes of the mouth and of the thyroid follicles (Plate VI, Figure 21). The pericardium was completely invaded and replaced by lymphoid cells (Plate VIII, Figure 26), the myocardium was invaded only slightly. Pressure from a large mass of lymphoid cells between the sclera and chorioid layers was primarily responsible for the exophthalmia (Plate V, Figure 19; Plate VI, Figure 20; Plate VII, Figure 27). The cells from this mass had proliferated into the surrounding regions through this pathway, invading the epichorioidal lymph space and the anterior chamber. The cornea was slightly thickened but there was very little involvement of the retina and other structures of the eye. Extension of the growth took place not only by local proliferation but also by way of the blood stream (Plate IX, Figure 33; Plate X, Figure 36) and in particular through the

lymph system. Blood vessels were constricted and invaded directly by lymphoid cells (Plate IX, Figure 33). Metastatic growths were present in the corium of the skin (Plate VII, Figure 24; Plate VIII, Figure 29), the gills (Plate VI, Figure 20; Plate VIII, Figure 28), the submucosa of the intestine (Plate IX, Figure 30), the liver (Plate IX, Figure 31), pancreas (Plate IX, Figures 32 and 33; Plate X, Figure 34), kidney (Plate X, Figure 35) and in the retroperitoneum (Plate IX, Figures 30, 32, and 33; Plate X, Figures 34, 36 and 37).

Many of these metastatic growths were not unlike the clinical subvarieties often reported for human lymphosarcomas. As in human lymphosarcoma, the testes were also a site of metastatic growth. The seminiferous tubules were considerably dilated but not entirely filled with sperms. That the germinal epithelium was still functioning was indicated by the presence of numerous spermatocytes in phases of meiosis in their transformation to the mature sperm. The pathological effects on the kidney were not unlike those present in the lymphosarcoma of the pike. Renal tubules and glomeruli were constricted or destroyed and the parenchyma entirely replaced with lymphoid elements. The submucosa of the intestine was packed solidly as should be expected since this region is one of the main lymphopoietic areas in fish. The process extended laterally, invading and destroying the muscularis. In some regions the growth was so extensive that pressure on the mucosa was sufficient to cause the intestinal lumen to be partially or completely occluded. The stomach was not affected. In humans, retroperitoneal lymphosarcoma is a characteristic of the disease. In *Astyanax*, the growth in this region is likewise extensive. The majority of the lymphoid cells were typical of those present in other areas, but in certain regions groups of smaller round cells also were found (Plate X, Figure 37).

A structure characteristic of the spleen was not seen. However, an encapsulated mass near the intestine was found which showed darkly staining lymphoid cells around numerous lighter staining germinal centers. Freely scattered throughout the mass were many erythrocytes, but typical blood vessels were at a minimum. The neoplastic growth also involved the pancreas, which in this fish, as in most teleosts, is a diffuse gland embedded in a loose connective tissue containing fatty tissue and numerous blood vessels. Each normal acinus consists of a single row of typically staining epithelial cells, resting on a delicate basement membrane and converging towards a central lumen often with centroacinar cells. The lymphoid growth had infiltrated throughout the gland (Plate IX, Figures 32 and 33), breaking through tl supporting membrane and disrupting tl orderly arrangement of the acini and the ducts. The acini that remained intact i variably showed dilated lumens (Plate I Figure 32), but more frequently they we broken up into isolated cells (Plate IX, Fi ure 33). The typical cytological appearan of the pancreatic cells was lacking. The e tire cell was basophilic and no zymogen gra ules were noted. Of interest is the fact th the Islet Gland, which is a distinct stru ture in these fishes, although surrounde by lymphoid cells, was not penetrated (Pla X, Figure 34). The liver was not involve extensively. In certain regions the liver s nuses were filled with lymphoid cells, b the parenchyma was invaded only slightl There was some collateral effect due to pre sure from the retroperitoneal masses ar constriction of the bile duct by the surroun ing neoplastic cells.

Histologically the cells involved in th lymphosarcoma in *Astyanax* were differe tiated lymphocytes supported by a delica reticulum. Most of the cells were round i appearance and more or less uniform i size, measuring about 3.5 microns in dian eter. They had very little visible cytoplas and the nuclei were hyperchromatic. In ce tain retroperitoneal masses (Plate X, Fi ure 37) nests of smaller lymphoid cell measuring about 1.5 microns, with dense staining nuclei, were present together wit the larger lymphocytes. Such masses showe the presence of the reticulum more clearl In most regions the reticulum was very de icate; in a few areas it was thickened co siderably. Frequent mitotic figures we found in all regions . There were no indic tions of inflammatory reaction, and regre sive changes were rare. Intranuclear c cytoplasmic inclusion bodies were not see

Discussion.

According to Feldman (1932), Boy (1939), Ewing (1940) and others, the seems to be little doubt that lymphosarcom is a true neoplasm. In the cases describe above the cells involved in the growths hav the power to infiltrate and destroy norma tissue. The presence of lymphoid cells lyin in the meshes of a delicate reticulum, nu merous mitoses, metastases and the absenc of evidence of an inflammatory process c leukemic condition indicate that the disease described for the pike and *Astyanax* fit int the category of lymphosarcoma.

Lymphosarcomas in human and othe mammals usually begin in lymph node However, such structures are not present i fishes, the lack of them being compensate by an abundance of lymphoid tissue in th submucosa, spleen, thymus, kidney an "head-kidney." In many teleosts, the kid

ney (mesonephros) is the main hemopoietic organ, the intertubular tissue resembling the lymphomyeloid tissue of spleen (Jordan and Speidel, 1924). However, this does not seem to be the case in the pike. This fish has a well developed "head-kidney," an enlarged portion of the anterior part of the kidney, which is almost entirely composed of lymphoid tissue that has replaced the renal elements. The exact function of this organ is not entirely understood. Sections stained with Giemsa's and Mallory's show a well developed reticulum, numerous free erythrocytes, sinusoids and lymphoid cells of various sizes with staining reactions indicating that this part of the kidney functions mainly in hemopoiesis. Similar lymphoid tissue is found in certain regions (subcapsular) of the kidney proper, particularly in the vicinity of the larger blood vessels. It should be emphasized that the primary site of the lymphosarcomas in the pike was invariably found in the posterior part of the kidney. It is probable that the origin of the lymphosarcoma is centered in these masses of lymphoid tissue within the kidney.

A thymus is present in many fishes, if not in the adults at least in the embryos. In *Astyanax* and closely related fishes (e. g. *Anoptichthys jordani* Hubbs and Innes, a blind relative living in caves of Mexico) there is a paired lymphoid structure lying in juxtaposition to the last gill arches in the posterior part of the branchial cavity (Plate XI, Figure 38). These structures may represent the thymus in these fishes. Histologically it is composed of closely packed lymphoid cells of uniform size and staining reaction supported by a delicate reticulum. The lymphoid cells from these "glands" extend out to the gill filaments and under certain conditions are massed in large numbers. It has been suggested that the function of these lymphoid structures is to protect the gills, by phagocytosis, from harmful microorganisms and other foreign objects that may be strained through them. The striking similarity of the lymphoid cells in the lymphosarcoma of *Astyanax* to those present in these thymus-like bodies and the fact that the latter are not present in the diseased fish, the major part of the growth being a large mass protruding from this area into the branchial cavity, lead one to suspect that they are the primary loci of the growth in this fish. Circumstantial evidence that this may be the case is afforded by an instance of simple lymphoid hyperplasia found in another specimen of *Astyanax*. This fish was kept in complete darkness for a period of three years for experimental purposes. Stained sections show a marked proliferation of lymphoid cells from the thymus-like bodies into the gills, tissues of the hyoid regions, and the thyroid (Plate XI, Figure 39). It may well be that here we have the beginning of the neoplastic process found in the *Astyanax* described above.[1]

It is well known, as pointed out by Ewing (1940), that "lymphoid tissue responds to irritation with inflammatory hyperplasia far more actively than any other tissue," and further that "lymphoid tissues are relatively mobile rather than fixed, and lymphocytes are not only ameboid but are structurally placed in easy access to lymph- and blood-paths. Hence tumors and tumor-like processes in lymphoid tissue are frequent and, as a rule, tend to become widely diffuse." However, the etiology of many of the lymphoid growths in humans and other animals is still unknown. In certain types, an infective agent is indicated (e.g. lymphosarcoma in dogs); in others (e.g. lymphoblastoma in chickens) an hereditary predisposition is suggested (Feldman, 1932). The etiology of the lymphosarcomas in the pike and in *Astyanax* is still unknown. The appearance of the disease in pike of different ages and sex living in the same tank, and at different intervals, seems to point to an infective agent. However, it is quite possible that the disease in both species of fishes may be due to nutritional or hormonal imbalance, since there is no histological or cytological evidence to indicate that an infectious agent and/or an infectious process is involved.

SUMMARY.

1. Lymphosarcomas are described from the pike, *Esox lucius* Linnaeus, and the Mexican characin *Astyanax mexicanus* (Filippi).

2. The kidney is the primary locus of the disease in the pike, with metastatic growths occurring in the liver, spleen and retroperitoneal tissues. In the characin, the thymus-like lymphoid structure is apparently the primary locus, with extensive local proliferation and metastatic growth occurring in practically every tissue and organ of the body. The normal histology of these structures is described relative to the lymphosarcomas.

3. The lymphoid cells involved in the growths differ in the two species. In the pike, the cells are mainly of the lympho-

[1] Another instance of lymphoid hyperplasia, approaching more closely the lymphosarcomatous condition herein described, has been studied. The specimen, a female measuring 25 mm. in standard length, was a third generation *Astyanax* of the same general stock as the others. The fish was four months old and had been kept in total darkness for two months, together with nineteen others, when killed and sectioned. There were no external manifestations of the disease. Histologically, however, the thymus-like bodies were enormously enlarged and protruded into the branchial cavity. There was some local proliferation into the gills, skin and other surrounding structures with some indications of involvement of certain internal organs (intestine, kidney). The "head-kidney" was exceptionally enlarged. The condition described here appears to be intermediate to the two cases reported above.

blast type; those in the characin are typical lumphocytes. In both cases, however, there is an extensive development of the reticulum and fibrous stroma. Numerous mitotic figures in various stages are present.

4. There is no histological or cytological evidence of an infectious agent, even though, in the case of the pike, twelve fish varying in age and sex living together in same tank were affected with the disease during a year period (1940-1941). The lymphosarcoma in the characin is an isolated case.

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EXPLANATION OF THE PLATES.

All photomicrographs, except Fig. 22, were taken of sections stained with hematoxylin-eosin.

LYMPHOSARCOMA IN THE PIKE, *Esox lucius*

PLATE I.

Fig. 1. Lymphosarcoma nodule in the kidney of the pike. Slightly less than natural size. Photographed by S. C. Dunton, Staff photographer of the New York Zoological Society.

Fig. 2. Metastatic nodules in the liver. ½ natural size. Photographed by S. C. Dunton.

Fig. 3. Section through the nodular growth of the kidney showing extensive proliferation of lymphoblasts, thickened and thrombosed blood-vessels. 75 ×.

Fig. 4. In some fish the nodular growth seen in Figure 1 is also associated with a granular type tissue. This figure is a section through such a growth. Many of the tubules are destroyed or replaced by the neoplastic cells. 150 ×.

PLATE II.

Fig. 5. Details of lymphoblast cells involved in the lymphosarcoma of the kidney. 675 ×.

Fig. 6. Another area of the kidney showing a nest of smaller lymphoid cells. 675 ×.

Fig. 7. Cells from the lymphosarcoma of the kidney. Note the mitotic figure. 675 ×.

Fig. 8. Neoplastic cells advancing on a renal tubule. 675 ×.

PLATE III.

Fig. 9. Renal tubule completely constricted and invaded by the neoplastic cells. 675 ×.

Fig. 10. Extension of the lymphosarcoma into the peripheral region of the kidney. Note the extensive development of reticulum. 75 ×.

Fig. 11. Same as Figure 10, except from another area. The appearance here is not unlike that of a follicular lymphoblastoma. 75 ×.

Fig. 12. Another region of the periphery of the kidney showing extensive development of fibrous tissue. 75 ×.

PLATE IV.

Fig. 13. Same as Figure 10 at higher magnification, showing cellular details. 675 ×.

Fig. 14. Epithelium of renal tubule invaded by lymphoid cells. 675 ×.

Fig. 15. Metastasized lymphoid elements in the liver. 350 ×.

Fig. 16. Details showing extensive development of fibrous tissue in liver, with liver cells arranged in cords resulting from pressure of the surrounding growth. 675 ×.

PLATE V.

Fig. 17. Spleen showing extensive development of "pulp cords." 75 ×.

Fig. 18. Infiltration of "pulp cord" material into surrounding fat. Note neoplastic cells in retroperitoneal area. 75 ×.

LYMPHOSARCOMA IN *Astyanax mexicanus.*

Fig. 19. Photograph of living fish showing external manifestations of the neoplastic disease. Note enlarged left opercular area and exophthalmia. About natural size. Photographed by S. C. Dunton.

PLATE VI.

Fig. 20. Section of the region of the left branchial cavity showing the large lymphoid mass protruding into the cavity. Note the involvement of all tissues at this level, including the brain. 75 ×.

Fig. 21. Section through the hyoid region showing involvement of the thyroid, mucous membrane and other structures of this area. 75 ×.

PLATE VII.

Fig. 22. Lymphosarcoma involving the bony and cartilaginous structures of the branchial region. Note the hyperplasia of cartilage. Mallory's stain. 75 ×.

Fig. 23. Lymphoid growth infiltrating the bony and muscle structures of the head region. 75 ×.

Fig. 24. Groups of lymphoid masses in the corium. 75 ×.

Fig. 25. Invasion of the epithelium of the skin by lymphoid cells. 675 ×.

PLATE VIII.

Fig. 26. Lymphosarcoma involving the pericardium. 156 ×.

Fig. 27. Lymphosarcoma mass between the sclera and chorioid region of the eye. 156 ×.

Fig. 28. Section through the gills and at the edge of the main lymphoid mass shown in Plate VI, Figure 20. 156 ×.

Fig. 29. Lymphoid cells infiltrating the structures at the tip of the snout. Note also the involvement of melanophores. 156 ×.

PLATE IX.

Fig. 30. Retroperitoneal masses of the lymphosarcoma in the region of the intestine. The submucosa is solidly packed with lymphoid cells. 75 ×.

Fig. 31. Nests of lymphoid cells in sinusoids of the liver. The hepatic cells and parenchyma are only slightly involved. 350 ×.

Fig. 32. The exocrine part of the pancreas is a diffuse gland, but its basic architecture is not unlike that found in higher vertebrates. In some areas, as shown here, the acini are still intact, but their lumens are dilated considerably and are invaded. 156 ×.

Fig. 33. In other regions the basement membrane supporting the epithelial cells of the acini is invaded, breaking up the structure into isolated cells. Note also the pinching-off effect on a blood vessel by the advancing growth. 350 ×.

PLATE X.

Fig. 34. The endocrine part of the pancreas is a distinct structure. Note that although it is surrounded by lymphoid cells, no penetration has taken place. 350 ×.

Fig. 35. Invasion of the kidney. Considerabl destruction of the renal tubules an glomeruli can be seen. 75 ×.

Fig. 36. Details of lymphoid cells from retrc peritoneal mass. Note the lymphoi cells in the blood. 675 ×.

Fig. 37. Details from retroperitoneal mas showing lymphocytes of two sizes. Th relationship between these cells is nc known. Note also the extensive deve opment of the reticulum. 675 ×.

PLATE XI.

Fig. 38. Section through one of the thymus like lymphoid structures found i *Anoptichthys jordani*, a close relativ of *Astyanax mexicanus* in which sim lar bodies occur. Note the relatior ships of this structure to the gills an surrounding tissue. 75 ×.

Fig. 39. An *Astyanax mexicanus* kept in th dark three years, showing an exter sive proliferation of the thymus-lik lymphoid tissue. In this section th hyoid region is completely invaded, ir volving and destroying tissues of thi region, including thyroid follicle 75 ×.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

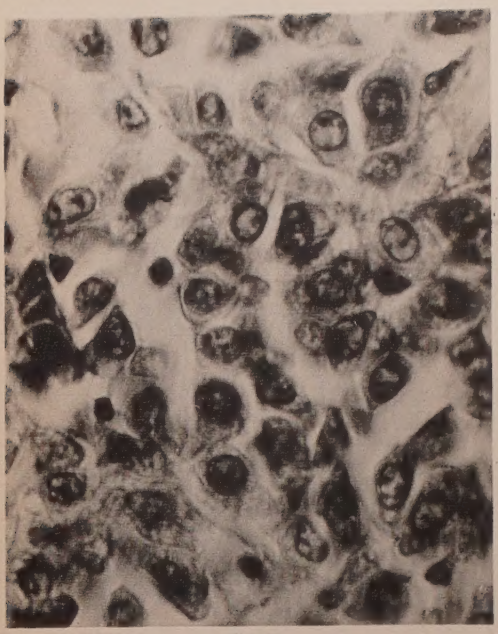

FIG. 5.

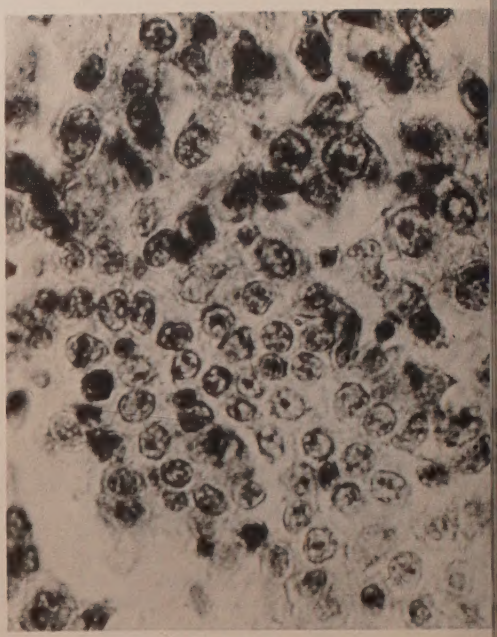

FIG. 6.

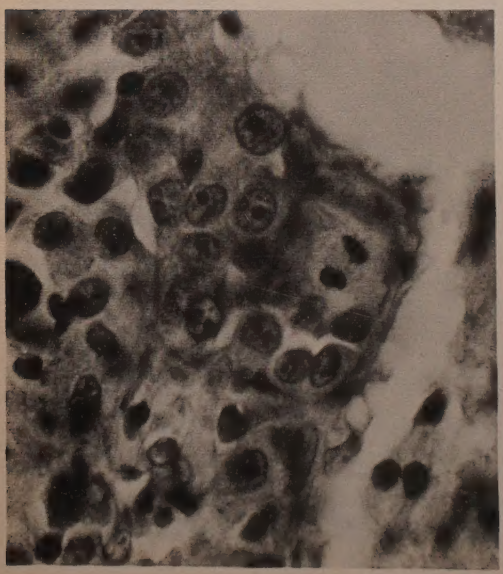

FIG. 7.

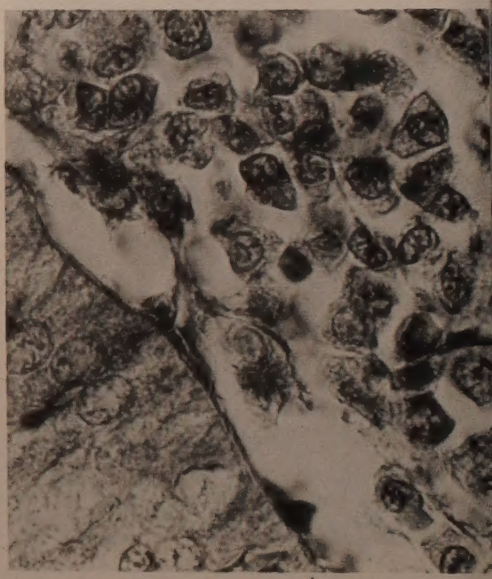

FIG. 8.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

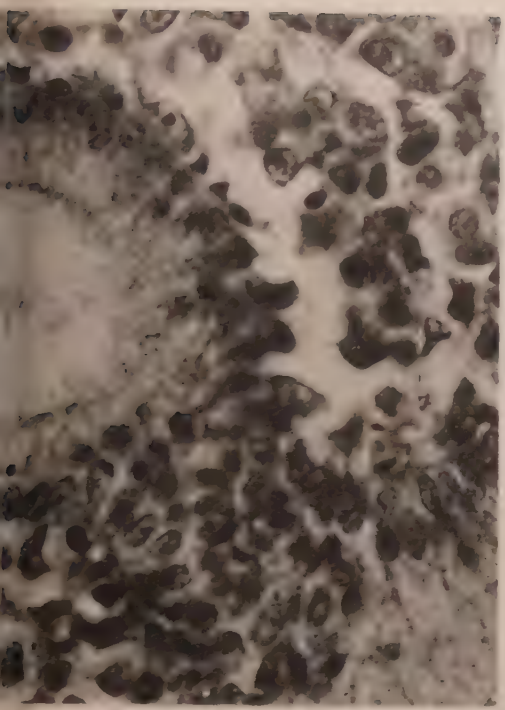

FIG. 9.

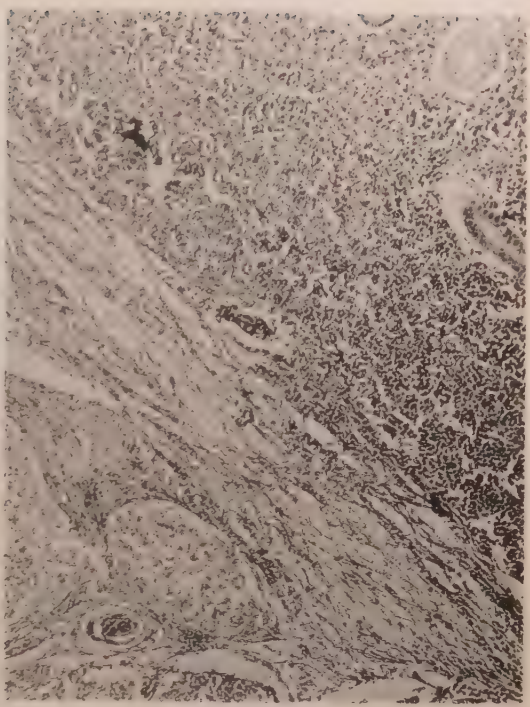

FIG. 10.

FIG. 11.

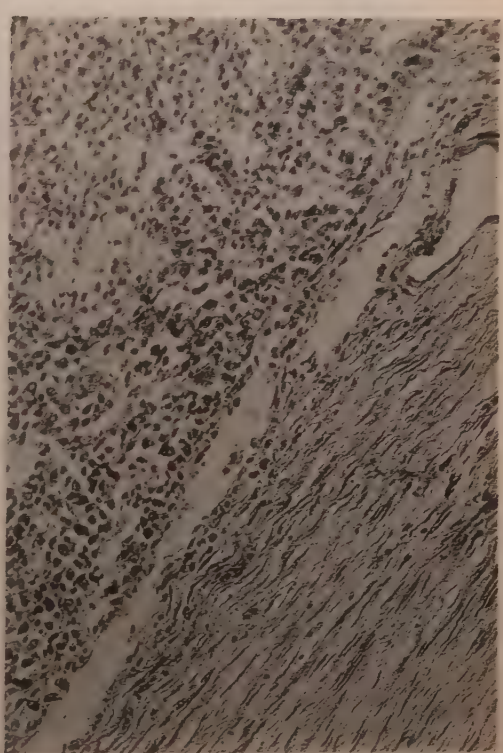

FIG. 12.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

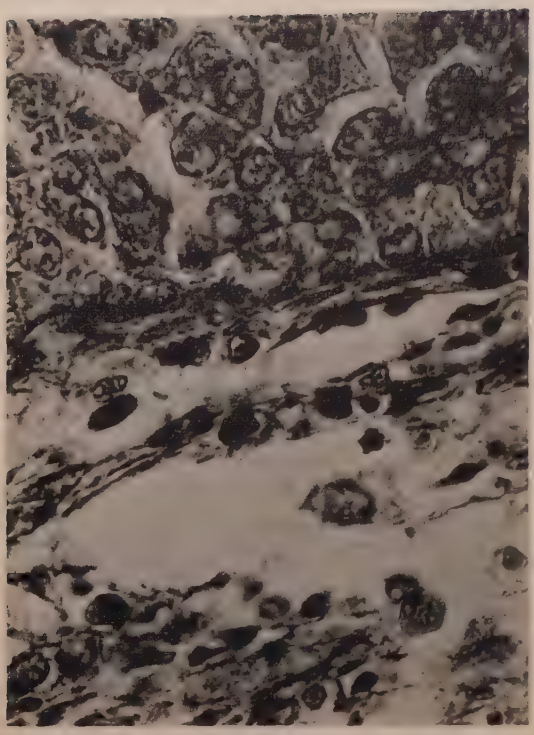

FIG. 13.

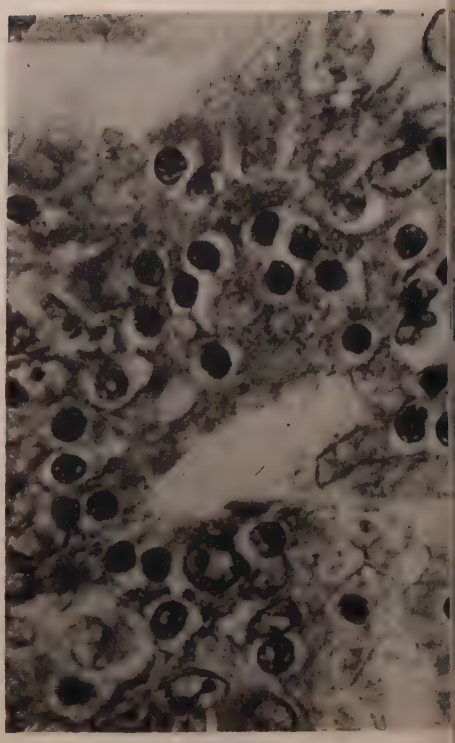

FIG. 14.

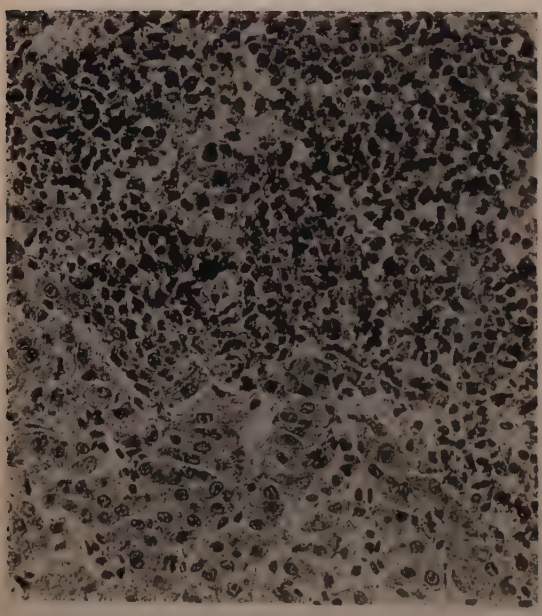

FIG. 15.

FIG. 16.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

FIG. 17.

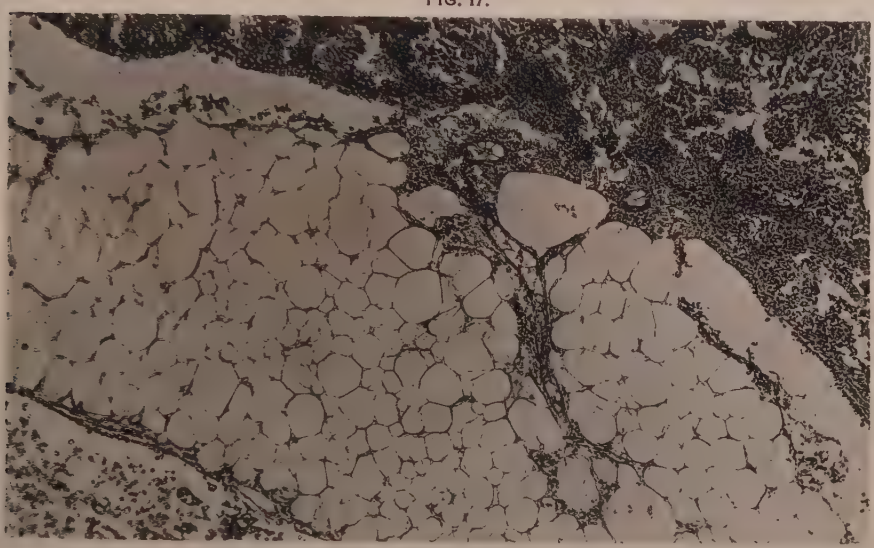

FIG. 18.

FIG. 19.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

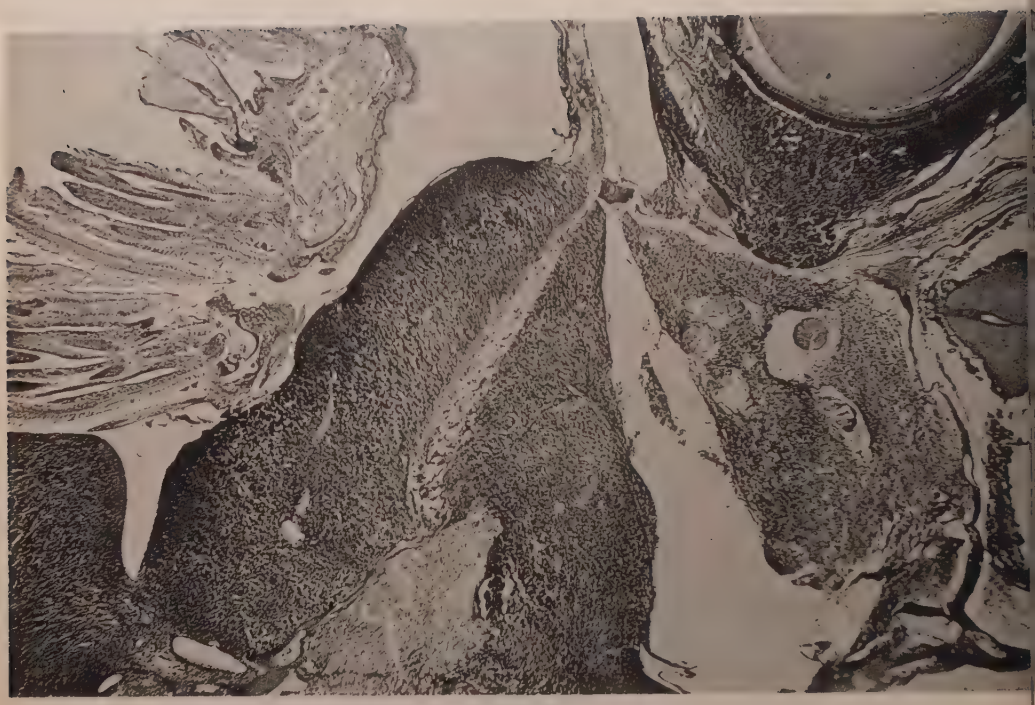

FIG. 20.

FIG. 21.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

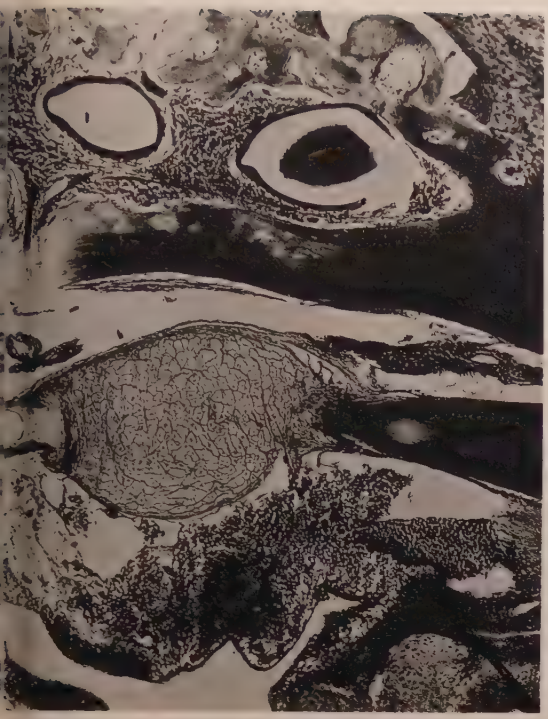

FIG. 22.

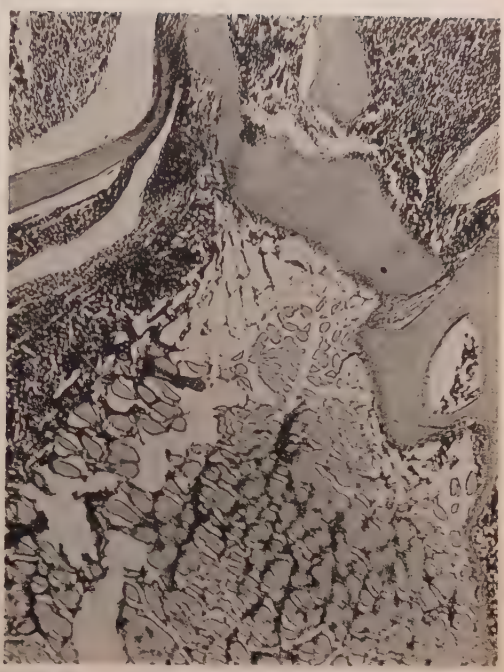

FIG. 23.

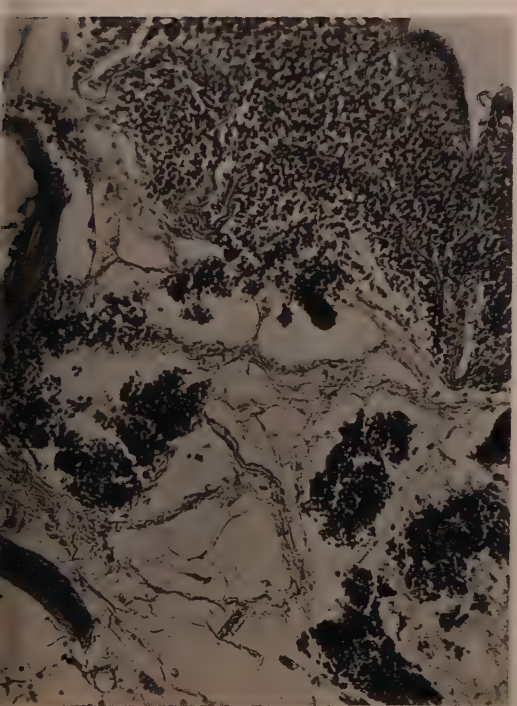

FIG. 24.

FIG. 25.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

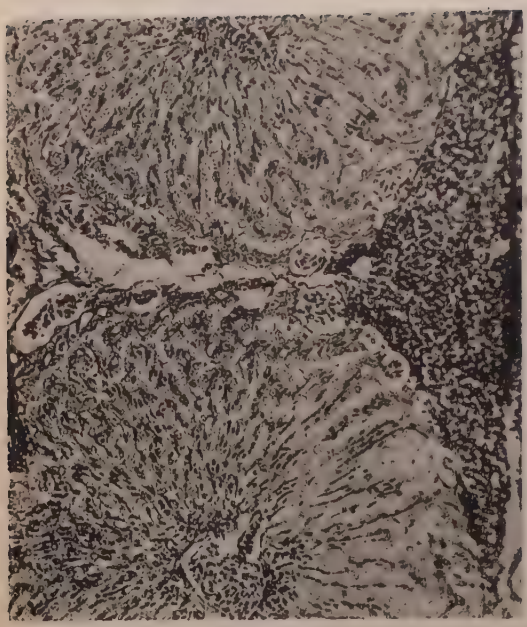

FIG. 26.

FIG. 27.

FIG. 28.

FIG. 29.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

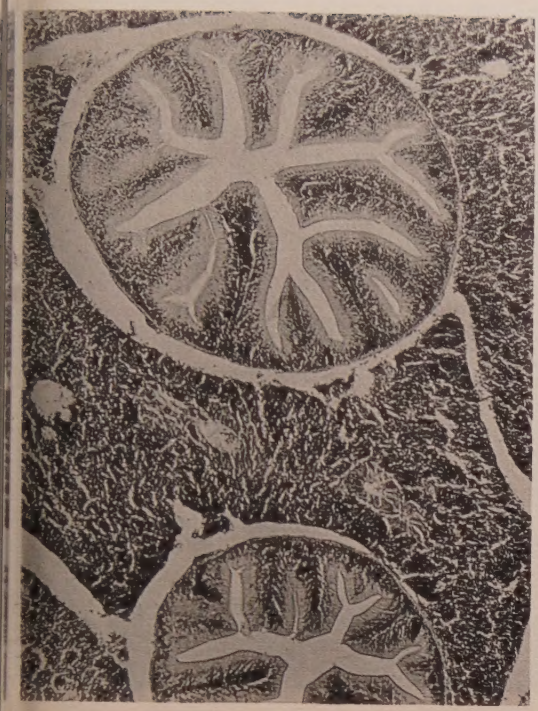

FIG. 30.

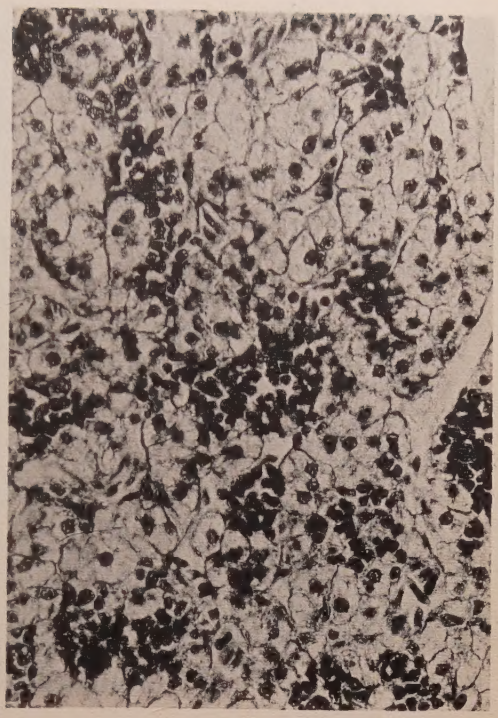

FIG. 31.

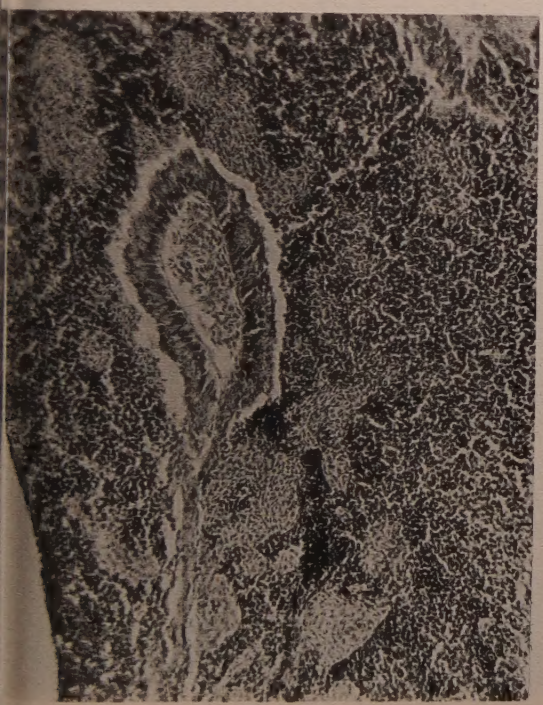

FIG. 32.

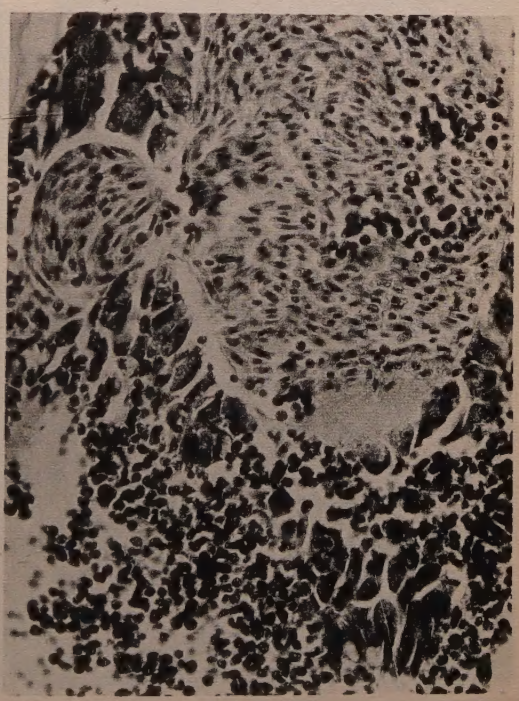

FIG. 33.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

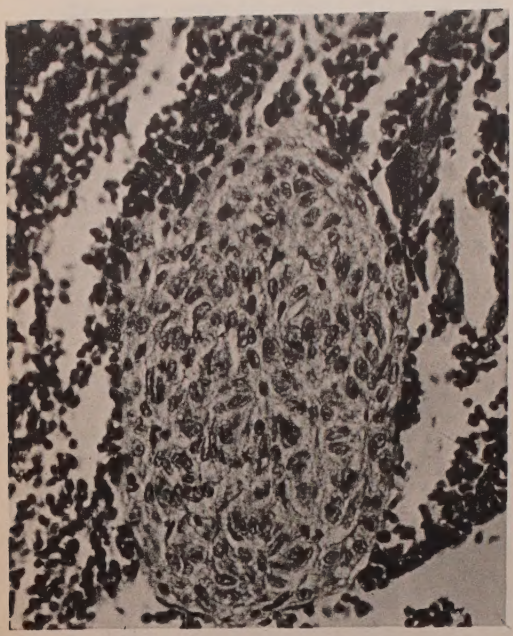

FIG. 34.

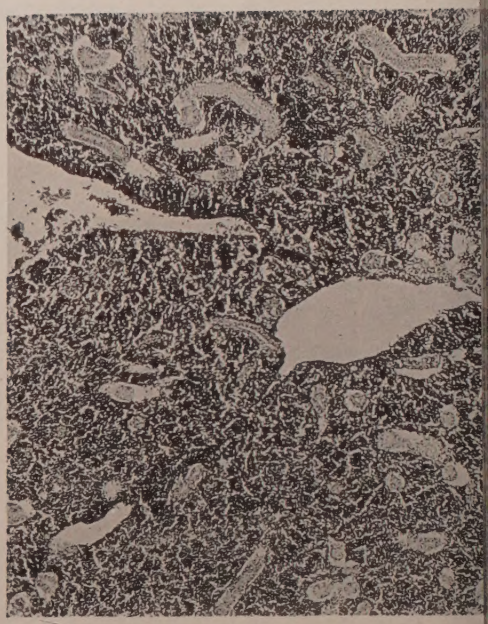

FIG. 35.

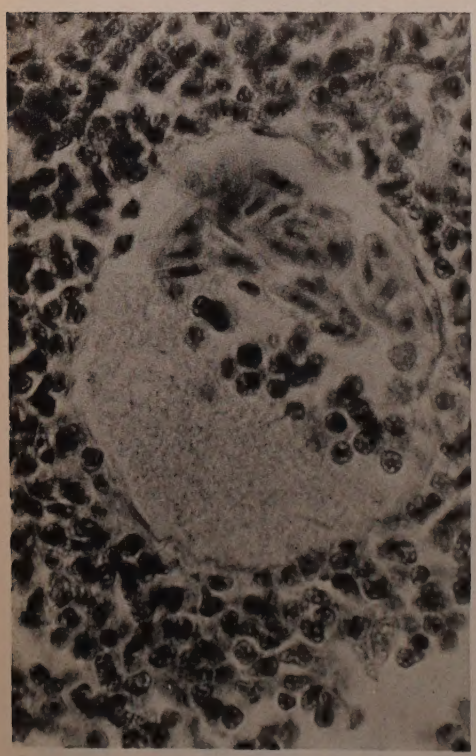

FIG. 36.

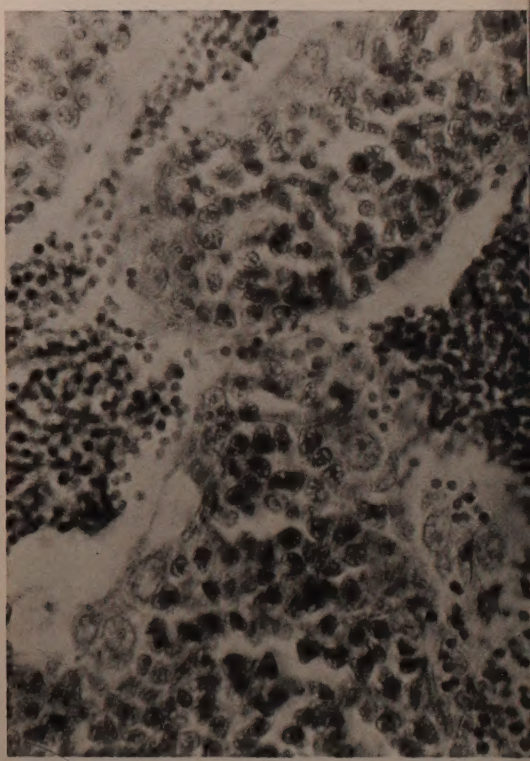

FIG. 37.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.

FIG. 38.

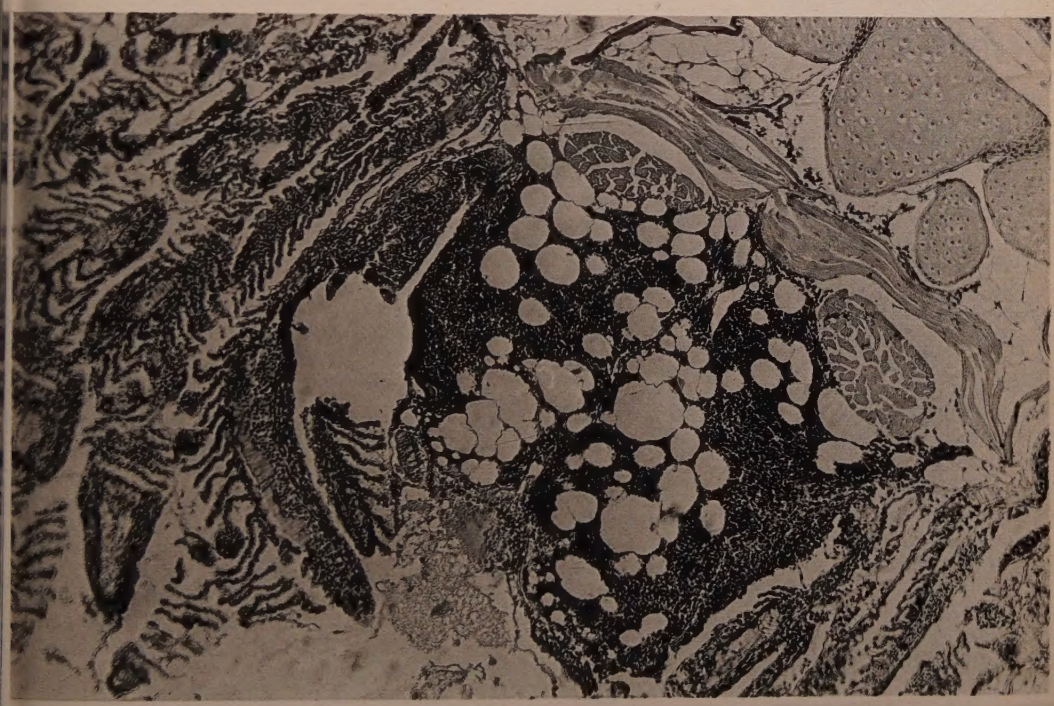

FIG. 39.

SPONTANEOUS NEOPLASMS IN FISHES. III. LYMPHOSARCOMA IN ASTYANAX AND ESOX.